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Causal interrogation of neuronal networks and behavior through virally transduced ivermectin receptors

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Abstract

© 2016 Obenhaus, Rozov, Bertocchi, Tang, Kirsch, Betz and Sprengel.The causal interrogation of neuronal networks involved in specific behaviors requires the spatially and temporally controlled modulation of neuronal activity. For long-term manipulation of neuronal activity, chemogenetic tools provide a reasonable alternative to short-term optogenetic approaches. Here we show that virus mediated gene transfer of the ivermectin (IVM) activated glycine receptor mutant GlyRα1AG can be used for the selective and reversible silencing of specific neuronal networks in mice. In the striatum, dorsal hippocampus, and olfactory bulb, GlyRα1AG promoted IVM dependent effects in representative behavioral assays. Moreover, GlyRα1AG mediated silencing had a strong and reversible impact on neuronal ensemble activity and c-Fos activation in the olfactory bulb. Together our results demonstrate that long-term, reversible and re- inducible neuronal silencing via GlyRα1AG is a promising tool for the interrogation of network mechanisms underlying the control of behavior and memory formation.

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Keywords

Glycine receptor, Ivermectin, Neuronal silencing, Odor discrimination, RAAV